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Effects of Long-Term Voluntary Wheel Exercise on Male and Female Wistar Rats

I. Longevity, Body Weight, and Metabolic Rate

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Abstract. Male and female Wistar rats (n = 140) age 1.5 months were maintained in either wheel-cage units or cage units for their entire life span. Voluntary wheel exercise significantly increased the mean longevity of both male and female rats compared with that of control rats. Between and within groups, growth duration was positively related to longevity, and growth rate was negatively related to longevity. These factors may explain differences in longevity between exercise and control groups and differences in longevity between male and female groups. These factors of growth, here defined in terms of body weight increment, may possibly account for many instances of group differences in longevity.

Webb et al. (1977) published a report of the physiological characteristics of a 77-year-old champion runner. Such reports indicate that some aged people may be able to respond to physical training with dramatically increased capabilities, such as increased lung capacity and metabolic rate. However, whether increased survival of older people or animals occurs as a result of exercise is not clear. Several animal studies have suggested this possibility (*McCay et al.*, 1941; *Retzlaff et al.*, 1966). The major positive finding (*Retzlaff et al.*, 1966) obtained significantly longer life spans for exercised groups than for nonexercised groups. However, some difficulties with this study were: control groups did not live a normal life span (15 months vs. the expected 20–25 months of most rat colonies (*Schlettwein-Gsell,* 1970), male and female control longevities did not differ – usually female rats liver longer than male rats (*Schlettwein-Gsell,* 1970) –, and exercised rats weighed more than control rats – exercised rats usually weigh less than nonexercised rats (*McCay et al.*, 1941; *Edington et al.*, 1972).

The present study is part of a long-term project to determine (a) group differences in longevity and aging patterns as a function of voluntary exercise; (b) different ages at which voluntary exercise may be effectively initiated to produce differential results in longevity and aging, and (c) factors which may act to change the level of voluntary exercise at maturity and during advanced old age. This report is concerned with longevity, body weight factors, and metabolic rate in male and female Wistar rats as a function of voluntary wheel exercise.

Method

Subjects

The subjects of this experiment were 140 male and female Wistar rats. These animals were all maintained in the same room with a constant temperature of 20–22 °C and with lights on from 6 a.m. to 6 p.m. and lights off from 6 p.m. to 6 a.m. The rats were fed Purina laboratory chow (or equivalent) and water *ad libitum.*

Procedure and Apparatus

At the age of 1.5 months, male and female rats were placed in either standard laboratory cages or activity wheels with attached cages. 2 rats of the same sex were placed within each wheel-cage unit or cage unit.[1] There were a total of 32 females and 28 males in standard laboratory cage units and 40 females and 40 males in exercise wheel-cage units. The laboratory cages were 17.5 cm wide, 28.0 cm deep, and 17.0 cm high.[2] The cages attached to the wheels were the same width and depth, but the height was less (15.0 cm) due to the positioning of the counter. The wheels were 35.0 cm high and 13.0 cm wide. All cages and wheels were constructed of stainless steel.

All rat pairs stayed in their respective environments until death. When 1 rat of a pair died, the remaining rat was alone until death. Wheel activity measures were obtained daily, but are not examined in detail in the present report.[3] Body weights were obtained weekly until 6 months of age, after which the rats were weighed monthly. Starting at 6 months of age and every 3 months thereafter, the metabolic rate (ml 0_2/g/h) was obtained for selected rats.[4] A spirometer system, described in a previous report (*Goodrick,* 1973), was used to obtain an accurate measure of oxygen consumption for each rat.

Data Analyses

Analyses of variance (unequal n) were computed for longevity, growth duration, growth rate, and peak weight. Each of these analyses of variance was a 2 × 2 design, sex (male vs. female) × caging condition (voluntary exercise vs. control). In addition, Pearson product-moment correlation coefficients (r) were obtained for 'longevity' and 'growth duration', 'longevity' and 'growth rate', and longevity' and 'peak weight' for each of the four groups (combinations of sex and caging).[5] Mean body weights are reported for

[1] The rats were paired during testing to double the number of rats in this experiment. This procedure resulted in a more efficient use of space and equipment, both of which are limited. Mean voluntary wheel exercise of paired male or female rats is the same or greater than obtained for singly housed male or female rats.

[2] At the Gerontology Research Center the rats are maintained throughout their lifespan in cages twice the width of the cages used in the present study with 4 males per cage or 5 females per cage.

[3] The voluntary wheel exercise (VWE) pattern over the life span was similar to that obtained in earlier studies (*Slonaker,* 1912). After placement in the wheels at 45 days of age, VWE increased, peaking at days 78–81 – males 7,074 revolutions/rat/day (RRD), females 9,413 RRD – then VWE slowly decreased with increasing age (days 246–249: males 2,036 RRD, females 4,626 RRD; days 446–449: males 963 RRD, females 2,352 RRD; days 646–649: males 665 RRD, females 992 RRD). 1 mile = 1,443 revolutions.

[4] Metabolic rate (ml O_2/g/h) was obtained in the morning when the rats were normally inactive and resting. This measure may be considered an estimate of resting metabolic rate. The apparatus is described in a previous report (*Goodrick,* 1973). During each test, rats were placed in the apparatus, allowed to adapt for 10–15 min and a 30-min record of oxygen consumption was obtained.

[5] The correlation of growth rates with peak body weight and growth duration may be biased because peak body weight and growth duration are used in the calculation of growth rate. Therefore, these correlations were not included. The correlations of peak body weight and growth duration were not significant and are also not given.

ages 1.5 through 27.0 months, as well as the number of animals remaining, the standard error of the mean, and the statistical significance between groups (exercise vs. control) at each age as determined by t tests. Also, an analysis of variance was computed based on the body weight of 12 randomly selected rats from each group (selecting only rats which lived to 21 months of age). This repeated measures analysis was a 2 × 2 × 7 design, sex (male vs. female) × caging condition (voluntary exercise vs. control) × age (3, 6, 9, 12, 15, 18 and 21 months).

An additional table reports the total number of rats alive and the number and percentage of rats which gained weight, were stable in weight, or lost weight from 9 to 27 months of age for each of the four groups of rats. Mean metabolic rates are presented for age 3 through 24 months, as well as number of rats tested, the standard errors of the mean, and the statistical significance between groups as determined by t tests. An analysis of variance was also computed based on metabolic rates of 12 rats from each group. The analysis was the same as for body weight.

Additional correlations were obtained of 'longevity' and 'body weight' at 1.5, 2.5, 3.5, 4.5, 6.0, 9.0 and 12.0 months of age for each of the four groups. In this report growth duration refers to the age in months at which peak body weight was attained, and growth rate refers to peak body weight divided by age (in months) when peak body weight occurs.

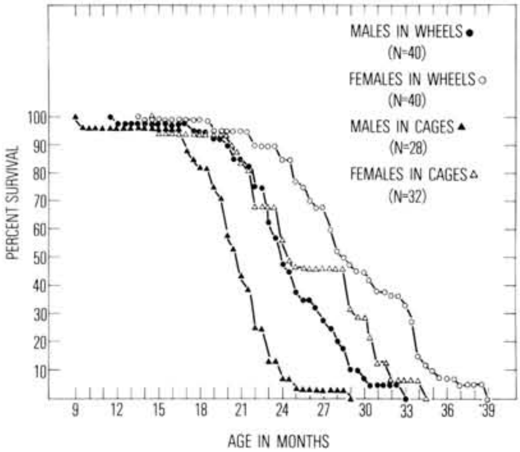

Fig. 1. Percentage survival as a function of age for male and female rats maintained in wheel-cage units or cage units.

Results

The results of voluntary wheel exercise were to increase significantly the mean life span of both male and female rats, compared with controls, F (1,136) = 5.34, $p < 0.01$ (table I; fig. 1). The mean life span of female rats was also significantly greater than the mean life span of male rats, F (1,136) = 10.89, $p < 0.01$ (table I), with the interaction of sex and caging condition not statistically significant. Mean growth rate was significantly slower for rats allowed voluntary wheel exercise than for controls, F (1,136) = 133.25, $p < 0.01$, and females grew more slowly than males, F (1,136) = 35.14, $p < 0.01$, with a significant interaction occurring due to a greater mean difference for male groups than for female groups (table I). Mean growth duration was significantly greater for rats allowed voluntary wheel exercise than for controls, F (1,136) = 8.59, $p < 0.01$, and females had a significantly longer mean growth duration than males, F (1,136) = 38.68, $p < 0.01$ (table I). Mean peak body weight was higher for controls than for those allowed voluntary wheel exercise, F (1,136) = 25.55, $p < 0.01$, and males had significantly higher mean peak body weights than females, F (1,136) = 94.58, $p < 0.01$ (table I). Interactions of sex and caging condition were not significant for growth duration and peak body weight.

Correlations of 'longevity' and 'growth rate' were all statistically significant, ranging from −0.43 to −0.57, and correlations between 'longevity' and 'growth duration' were all statistically significant, with correlations ranging from + 0.47 to + 0.74 (table II). For 'longevity' and 'peak body weight', correlations were statistically significant for male groups, but not

Table I. Means and standard errors of longevity, growth rate, growth duration, and peak body weight for male and female rats as a function of voluntary wheel exercise

	n	Longevity, months	Growth rate	Growth duration months	Peak body weight, g
Male					
Control	28	20.7 ± 0.6	51.2 ± 1.4	13.5 ± 0.4	677.3 ± 9.2
Exercise	40	24.7 ± 0.7	35.4 ± 1.1	16.1 ± 0.4	555.5 ± 6.3
Female					
Control	32	26.2 ± 0.8	24.6 ± 0.9	19.3 ± 0.5	463.6 ± 8.6
Exercise	40	29.2 ± 0.8	17.6 ± 0.6	22.4 ± 0.6	386.5 ± 2.0

Table II. Correlations of 'longevity and peak weight', 'longevity and growth duration' and 'longevity and growth rate' for each of four groups of rats

	Longevity × growth rate	Longevity × growth duration	Longevity × peak weight
Male			
Control	–0.43**	+ 0.51*	+ 0.39**
Exercise	–0.57*	+ 0.47*	+ 0.73*
Female			
Control	–0.54*	+ 0.74*	+ 0.11
Exercise	–0.46*	+ 0.60*	+ 0.06

* $p < 0.01$; ** $p < 0.05$.

for female groups (table II) although all correlations were positive.

Mean body weights, number of rats and standard errors are given in table III for each group from 1.5 to 27 months of age. At the start of the study, weight differences were not significant when control rats were compared with rats assigned to voluntary wheel exercise. However, mean body weights were significantly greater for control rats than for rats allowed voluntary wheel exercise at every age after the start of the study (2.5 through 24.0 months), except for the last age (27.0 months).

The repeated-measures analysis based on body weight measures of the same animals at all ages revealed highly significant effects, with mean body weight of rats allowed voluntary wheel exercise lower than mean body weight of control rats, $F(1,44) = 68.00$, $p < 0.01$, and mean body weight of female rats lower than

Table III. Number of rats, mean body weights, and standard errors as a function of voluntary wheel exercise for male and female Wistar rats

	Age, months											
	1.5	2.5	3.5	4.5	6.0	9.0	12.0	15.0	18.0	21.0	24.0	27.0
Male												
Control												
n	28	28	28	28	28	28	28	28	25	15	2	1
M	182.0	365.2*	446.8*	499.1*	535.1*	641.9*	660.6*	658.5*	615.2*	553.2*	552.2*	475.0
SE	3.0	4.7	5.7	6.7	8.0	6.9	7.8	12.8	16.7	24.3	8.5	–
Exercise												
n	40	40	40	40	40	40	40	38	38	34	23	10
M	177.7	329.1	373.4	424.5	447.7	514.4	534.1	547.9	538.3	514.2	489.7	477.0
SE	3.7	4.7	5.0	5.6	6.1	7.1	7.3	6.7	6.5	6.7	9.2	9.6
Female												
Control												
n	32	32	32	32	32	32	32	32	32	23	18	15
M	145.8	226.4*	261.9*	278.2*	301.3*	349.5*	365.7*	426.1*	443.4*	449.6*	428.4*	404.0
SE	1.5	2.2	2.6	8.7	4.8	5.6	6.2	10.0	9.5	10.8	13.0	18.2
Exercise												
n	40	40	40	40	40	40	40	39	38	36	34	24
M	146.5	210.8	238.3	259.0	271.1	296.8	313.5	328.7	342.4	362.0	367.0	384.7
SE	1.9	2.2	2.5	2.6	2.8	3.8	3.8	4.5	5.6	5.7	6.2	24.6

* $p < 0.01$, control vs. exercise.

mean body weight of male rats, $F(1,44) = 438.54$, $p < 0.01$. The second order interaction of caging condition, sex, and age was also significant, $F(6,264) = 16.64$, $p < 0.01$ (fig. 2), due to differences between male and female control or exercised rats differing with increasing age. Body weight differences between control rats and rats allowed voluntary wheel exercise were greatest for male rats at the middle portion of the life span (9, 12 and 15 months), but were greatest for female rats later in the life span (15, 18 and 21 months).

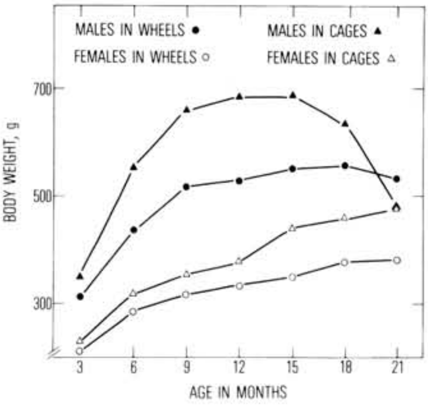

Fig. 2. Body weight as a function of age for male and female rats maintained in wheel-cage units or cage units.

This difference in body weight increment and decrement for the four groups is clearly shown in table IV, where the total number of

Table IV. Total number of rats, and number and percentage of rats that gained weight, were stable in weight, or lost weight as a function of sex and voluntary exercise for rats 9–27 months of age

Age, months	Total	Gain of 5 g or more		± 4 g		Loss of 5 g or more	
		n	%	n	%	n	%
Male: Exercise							
9	40	40	100.0	0	0.0	0	0.0
12	40	36	90.0	4	10.0	0	0.0
15	39	33	84.6	3	7.7	3	7.7
18	38	10	26.3	12	31.6	16	42.1
21	34	3	8.8	5	14.7	26	76.5
24	23	1	4.3	2	8.7	20	87.0
27	10	0	0.0	0	0.0	10	100.0
Male: Control							
9	28	28	100.0	0	0.0	0	0.0
12	28	23	82.1	4	14.3	1	3.6
15	28	13	46.4	2	7.2	13	46.4
18	25	2	8.0	4	16.0	19	76.0
21	14	0	0.0	1	7.1	13	92.9
24	2	0	0.0	0	0.0	2	100.0
27	1	0	0.0	0	0.0	1	100.0
Female: Exercise							
9	40	39	97.5	1	2.5	0	0.0
12	40	38	95.0	1	2.5	1	2.5
15	39	35	89.7	3	7.7	1	2.6
18	38	28	73.7	8	21.0	2	5.3
21	36	29	80.6	4	11.1	3	8.3
24	34	14	41.2	6	17.6	14	41.2
27	25	9	36.0	8	32.0	8	32.0
Female: Control							
9	32	32	100.0	0	0.0	0	0.0
12	32	30	93.8	2	6.2	0	0.0
15	32	31	96.9	0	0.6	1	3.1
18	32	27	84.4	1	3.1	4	12.5
21	23	12	52.2	3	13.0	8	34.8
24	18	2	11.1	2	11.1	14	77.8
27	15	1	6.6	1	6.7	13	86.7

Table V. Correlations of 'longevity' and 'body weight' as a function of age, sex, and voluntary wheel exercise

	n	Age, months						
		1.5	2.5	3.5	4.5	6.0	9.0	12.0
Male								
Control	28	−0.02	+0.05	+0.09	+0.11	+0.17	+0.16	+0.12
Wheel	40	+0.34	−0.02	−0.04	−0.15	−0.14	−0.02	−0.12
Female								
Control	32	−0.08	−0.23	−0.21	−0.20	−0.21	−0.33	−0.27
Wheel	40	−0.02	+0.03	−0.23	−0.23	−0.19	−0.34	−0.23

Table VI. Number of rats, mean metabolic rate (ml O_2/g/h × 100), and standard errors as a function of voluntary wheel exercise for male and female Wistar rats

		Age, Months							
		3	6	9	12	15	18	21	24
Male									
Control	n	12	12	12	12	12	12	12	–
	M	99.2	91.5*	88.2*	82.3*	77.8*	78.4*	74.2*	–
	SE	4.1	3.6	2.2	2.2	1.7	3.0	1.8	–
Exercise	n	12	40	40	40	38	38	34	20
	M	94.8	100.9	95.3	99.3	97.3	97.8	100.4	96.4
	SE	4.8	1.5	1.7	1.8	2.2	2.2	1.7	4.8
Female									
Control	n	12	12	12	12	12	12	23	16
	M	121.4	116.8*	119.9	110.1*	107.6*	107.7*	101.1*	103.4*
	SE	6.4	2.8	4.1	2.0	2.4	2.4	2.5	3.2
Exercise	n	12	40	40	40	39	38	36	30
	M	115.7	124.1	124.0	118.1	127.4	119.7	118.2	118.7
	SE	3.8	1.9	2.6	1.6	2.7	2.4	1.8	3.2

* $p < 0.01$, control vs. exercise,

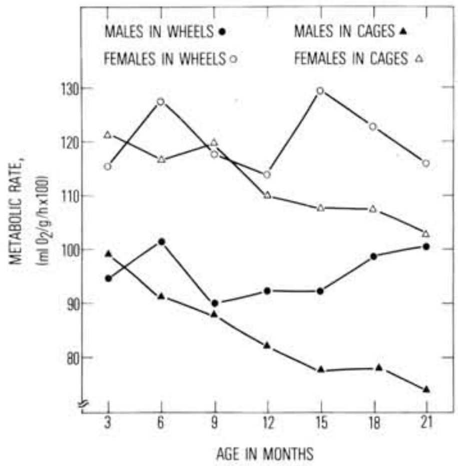

Fig. 3. Metabolic rate as a function of age for male and female rats maintained in wheel-cage units or cage units.

rats from age 9 to 27 months is shown, along with the number and percentage of rats that gained 5 or more grams, remained at ± 4 grams, or lost 5 or more grams. Rats allowed voluntary exercise continued to increase body weight over a longer period of the life span and compared with controls, did not begin to lose weight until much later in the life span.

Correlations of 'longevity' and 'body weight' from 1.5 to 12.0 months of age are shown in table V. Although 20 of 28 of these correlations were negative, 10 of these were less than −0.20, too low to have much predictive significance.

Mean metabolic rates for all rats measured are given in table VI. For both male and female groups, the mean metabolic rates of rats allowed voluntary exercise were significantly higher than the metabolic rates of control rats at all ages from 12 to 21 months. At the earliest age, 3 months, differences were statistically significant. A repeated measures analysis of variance using 12 subjects in each group was also computed with means shown in figure 3. Female rats had higher mean metabolic rates than male rats, $F(1,44) = 253.52$, $p < 0.01$ and rats allowed voluntary wheel exercise had higher mean metabolic rates than control rats, $F(1,44) = 34.81$, $p < 0.01$. Although mean metabolic rate decreased with increasing age, $F(6,264) = 5.98$, $p < 0.01$, the interaction between caging condition and age was significant, $F(6,264) = 8.55$, $p < 0.01$. For rats allowed voluntary wheel exercise, metabolic rate did not decrease with increasing age; metabolic rate decreased with increasing age only for control rats.

Discussion

The present results agree with the results of *Retzlaff et al.* (1966) in that exercise acts to retard the aging process. The mean longevity of the female rats allowed voluntary exercise was 3 months (11.5%) longer than the mean longevity of control female rats while the mean longevity of the male rats allowed voluntary exercise was 4 months (19.3%) longer than the mean longevity of the control male rats. Controls used in these comparisons were from populations housed within cage units in the same room as the rats housed within wheel-cage units, and the mean longevities for both male and female control rats were similar to those of other populations in our central colony (GRC, NIA, unpubl. data) and other rat colonies (*Schlettwein-Gsell,* 1970). The expected sex difference in longevity was obtained in the present rat populations, with female rats living longer than male rats (*Schlettwein-Gsell,* 1970), and body weights of rats allowed voluntary wheel exercise were lower than body weights of control rats as found in previous research (*Slonaker,* 1912; *McCay et al.,* 1941; *Edington et al.,* 1972). These results indicate that it is highly probable that rats allowed voluntary wheel exercise throughout their life span will live longer than rats not allowed voluntary wheel exericse.

Sacher (1959) suggested a positive relation between body weight and longevity, based on estimates of the body weight and maximal life span of 63 species, with high positive correlations of 'body weight' and 'longevity' indicating greater longevity for species with higher body weight. *Everitt and Webb* (1957) and *McCay et al.* (1941) obtained statistically significant positive correlations of 'body weight' and 'longevity' (r = +0.51 and +0.48, respectively), findings which support *Sacher*'s hypothesis. In the present study, within-group correlations of 'peak body weight' and 'longevity' were all positive, and were statistically significant for male groups, but not female groups. However, an inverse relation of peak body weight and longevity was found between groups in the present study. Female rats, lower in peak body weight than male rats, lived longer than male rats, and rats allowed voluntary wheel exercise, lower in peak body weight than control rats, lived longer than control rats. Similar contradictory evidence has been obtained for populations of inbred, hybrid, and mutant mice with respect to the relation of peak body weight and longevity between groups (*Goodrick*, 1977, 1978).

Much reported research concerns the relationship of body weight increment over time (growth rate) and longevity. *McCay and Crowell* (1934) originally presented data which supported the hypothesis that a slow rate of growth (through a reduction of food rations) leads to an increment in longevity compared with longevity of control groups growing at a faster rate (food *ad libitum*). Each of the present four groups had significant positive correlations of 'growth duration' and 'longevity' and significant negative correlations of 'growth rate' and 'longevity'. The lower the rate of growth and the longer the growth duration, the greater the longevity. These results are entirely consistent with the above hypothesis and data of *McCay* and his co-workers (*McCay et al.*, 1935, 1939).

Important additional evidence which suggests that growth factors rather than exercise factors are causal for increased longevity was obtained from the data of *Retzlaff et al.* (1966). Calculations based on the raw scores presented in their tables yield, for each of four groups (male-exercise, male-control, female-exercise, female-control) significant negative correlations for 'growth rate' and 'longevity' and significant positive correlations for 'growth duration' and 'longevity'.

Since growth rate was lower and growth duration longer for females than for males, and the former also lived longer than the latter, these sex differences further emphasize the importance of growth in the prediction of longevity. Women also live significantly longer than men; thus, an important hypothesis to be tested concerns whether human sex differences in longevity may also be related to differences in growth duration or growth rate.

The present data do not confirm the findings of *Ross and Bras* (1975) and *Ross et al.* (1976) with respect to their significant negative correlations of body weight and life span. *Everitt and Webb* (1957) also failed to obtain significant correlations of 'body weight' and 'longevity' early in the life span, although a significant positive correlation was obtained at 400 days of age for 'body weight' and 'longevity'.

Growth rate and growth duration factors, however, are confirmed as being of crucial importance in the prediction of life span. Highly significant positive correlations of 'growth duration' and 'longevity' were found in the present study for all four rat populations ranging from + 0.47 to + 0.74. *Everitt and Webb* (1957) obtained their highest correlation coefficient of + 0.62 for 'growth duration' and 'longevity' and *Ross et al.* (1976) obtained their highest correlation coefficient of + 0.48 for the 'time to double a body weight of 250 g' and 'longevity'. These findings all support the hypothesis and research results of *McCay et al.* (1934, 1935, 1939) that a long, slow period of body weight increment results in greater longevity than a short, fast period of body weight increment. Only the results of *Sherman and Campbell* (1935) fail to support the hypothesis; they did not find a significant difference in growth rates from 5 to 8 weeks of age for the rats that lived for short or long periods.

The groups of rats of the present study were genetically heterogeneous rats, as were the rats of *Retzlaff et al.* (1966), *Everitt and Webb* (1957) and *Ross et al.* (1976). Further evidence of the generality and importance of growth in relation to longevity was obtained in studies of genetically homogeneous inbred, hybrid, and mutant mice (*Goodrick*, 1977, 1978). In a study of body weight change over the life span and longevity, C57BL/6J mice and four mutations which differed in body weight were studied (*Goodrick*, 1977). Within each of these five mouse groups 'growth duration' and 'longevity' were positively correlated (r ranging from + 0.56 to + 0.86), and 'growth rate' and 'longevity' were negatively correlated (r ranging from −0.26 to −0.88). A second study (*Goodrick*, 1978) used inbred A/J and C57BL/6J mice, and F_1 hybrids (A/J X C57BL/6J) fed low or normal protein diets; there were six groups with 50 mice in each group. Correlations of 'growth rate' and 'longevity' were all negative and statistically significant for five of the six groups (r ranging from −0.36 to −0.67) and correlations of 'growth duration' and 'longevity' were all positive and statistically significant for five of the six groups (r ranging from + 0.36 to + 0.67). In these two studied combined, for the 11 groups, correlations of 'peak body weight' and 'longevity' were all positive and mostly low (r ranging from + 0.09 to + 0.80), although four attained statistical significance ($p < 0.05$). The results for a number of different genetically homogeneous mouse populations and several heterogeneous rat groups indicate that growth rate and growth duration factors have generality in the prediction of longevity.

Sacher (1977), in his review of factors which may act to prolong life, concluded that just two nonpharmacological treatments had been found to prolong life; caloric restriction in rats and reduction of body temperature for poikilotherms (*Sacher*, 1977, p. 628). These factors were explained by *Sacher* (1977, p. 628) '... as a consequence of a decrease of the rate of energy metabolism ...'. In the present study, metabolic rate (ml O_2/g/h $\times$ 100) was highest for the group of rats with the longest mean life span, while metabolic rate was lowest for the group of rats with the shortest mean life span. Metabolic rate of control groups decreased with increasing age, a finding also obtained for the basal metabolic rate in normal men (*Shock and Yiengst*, 1955). The explanation of *Tzankoff and Norris* (1977) of basal metabolic rate decrement with age in men as a correlated decrement in muscle mass can also be applied to control rats. Rats allowed voluntary wheel exercise may maintain muscle mass and not accumulate as much fat with increasing age and thus show less decrement in metabolic rate. The sex difference in metabolic rate (females higher than males) may also be due to a proportionally greater muscle mass per unit body weight for female rats than for male rats. It is well established that female rats are more active than male rats (*Slonaker*, 1912), a factor which may result in the suggested sex difference in muscle mass per unit body weight. The reversal of these differences for human males and females (*Boothby et al.*, 1936), with males having higher metabolic rates than females, may be due to either species and sex differences in body constitution, or cultural sex differences in human physical training. For rats tested at higher temperatures than in the present study, metabolic rate increased at advanced ages (*Kleiber et al.*, 1956; *Ring et al.*, 1967), findings which differ from the present study. Further studies with temperature and age as variables may be required to reconcile these differences.

Conclusions

The major findings of this experiment were the significant increases in longevity of rat groups allowed voluntary wheel exercise throughout the life span when compared with control groups not allowed voluntary wheel exercise. Both between groups and within groups, growth rate was negatively related to longevity and growth duration was positively related to longevity. Although groups lower in peak body weight had increased longevity, within groups peak body weight was positively correlated with longevity. Body weight from 1.5 to 12 months of age was not significantly related to longevity. Energy metabolism was higher in female rats than male rats and higher in rats allowed voluntary exercise than in control rats, with rats allowed voluntary exercise maintaining a high level of energy metabolism late in their life span, compared with controls. Male versus female differences in longevity as well as exercise versus control differences in longevity may be due to differences between groups in growth duration and/or growth rate.

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References

Boothby, W.; Berkson, J., and Dunn, H.: Studies of the energy of metabolism of normal individuals. A standard for basal metabolism, with a nomogram for clinical application. Am. J. Physiol. *116:* 468–484 (1936).

Chesky, J. and Rockstein, M.: Life span characteristics in the male Fischer rat. Expl Aging Res. *2:* 399–407 (1976).

Edington, D.; Cosmas, A., and McCafferty, W.: Exercise and longevity. Evidence for a threshold age. J. Geront. *27:* 341–343 (1972).

Everitt, A. and Webb, C.: The relation between body weight changes and life duration in male rats. J. Geront. *12:* 128–135 (1957).

Goodrick, C.: The effects of dietary protein upon growth of inbred and hybrid mice. Growth *37:* 355–367 (1973).

Goodrick, C.: Body weight change over the life span and longevity for C57BL/6J mice and mutations which differ in maximal body weight. Gerontology *23:* 405–413 (1977).

Goodrick, C.: Body weight increment and length of life. II. The effect of genetic constitution and dietary protein. J. Geront. *33:* 184–190 (1978).

Kleiber, M.; Smith, A., and Chernikoff, T.: Metabolic rate of female rats as a function of age and body size. Am. J. Physiol. *186:* 9–12 (1956).

McCay, C. and Crowell, M.: Prolonging the life span. Scient. Mon., N.Y. *39:* 405–414 (1934).

McCay, C.; Crowell M., and Maynard, L.: The effect of retarded growth upon the length of life span and upon the ultimate body size. J. Nutr. *10:* 63–79 (1935).

McCay, C.; Maynard, L.; Sperling, G., and Barnes, L.: Retarded growth, life span, ultimate body size and age changes in the albino rat after feeding diets restricted in calories. J. Nutr. *18:* 1–25 (1939).

McCay, C.; Maynard, L.; Sperling, G., and Osgood, H.: Nutritional requirements during the latter half of life. J. Nutr. *21:* 45–60 (1941).

Retzlaff, E.; Fontaine, J., and Furuta, W.: Effect of daily exercise on life span of albino rats. Geriatrics *21:* 171–177 (1966).

Ring, G.; Dupuch, G., and Creed, J.: The effect of voluntary exercise on the resting oxygen consumption of rats. Gerontologia *13:* 194–199 (1967).

Ross, M. and Bras, G.: Food preference and length of life. Science *190:* 165–167 (1975).

Ross, M.; Lustbader, E., and Bras, G.: Dietary practices and growth responses as predictors of longevity. Nature, Lond. *262:* 548–553 (1976).

Sacher, G.: Relation of life span to brain weight and body weight in mammals; in Wolstenholme and O'Connor, The life span of animals (Little, Brown, Boston 1959).

Sacher, G.: Life table modification and life prolongation; in Finch and Hayflick The biology of aging (Van Nostrand Reinhold, New York 1977).

Schlettwein-Gsell, D.: Survival curves of an old age rat colony. Gerontologia *16:* 111–115 (1970).

Sherman, H. and Campbell, H.: Rate of growth and length of life. Proc. natn. Acad. Sci. USA *21:* 235–239 (1935).

Shock, N. and Yiengst, M.: Age changes in basal respiratory measurements and metabolism in males. J. Geront. *10:* 31–40 (1955).

Slonaker, J.: The normal activity of the albino rat from birth to natural death, its rate of growth and the duration of life. J. Anim. Behav. *2:* 20–42 (1912).

Tzankoff, S. and Norris, A.: The effect of muscle mass decrease on age-related BMR changes. J. appl. Physiol. *43:* 1001–1006 (1977).

Tzankoff, S.; Robinson, S.; Pyke, F., and Brawn, C.: Physiological adjustments to work in older men as affected by physical training. J. appl. Physiol. *33:* 346–350 (1972).

Webb, J.; Urner, S., and McDaniels, J.: Physiological characteristics of a champion runner. Age 77. J. Geront. *32:* 286–290 (1977).

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